HFI-35

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region T1760M

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6009

May 8, 1998

WARNING LETTER

CERTIFIED MAIL –
RETURN RECEIPT REQUESTED

Lawrence Hoffman, Vice President & CFO
ImmunoGenetics, Inc.
711 Harding Hwy
Buena, New Jersey 08310

Dear Mr. Hoffman: **File No.: 98-NWJ-23**

During an inspection of your manufacturing facility located at 711 Harding Hwy., Buena, New Jersey from February 26 through March 16, 1998, it was determined that your firm manufactures veterinary products, including drugs. Veterinary drug products are defined the same as human drugs in Section 201 of the Federal Food, Drug, and Cosmetic Act (the Act).

During this inspection, Investigators collected samples of drug products for analysis and documented deviations from Current Good Manufacturing Practice Regulations (cGMPs), Title 21, Code of Federal Regulations (CFR), Parts 210 & 211. These deviations were noted on the Form FDA483, List of Inspectional Observations, issued to you at the close of the inspection.

The above stated inspection revealed that drug products manufactured at your facility are considered adulterated within the meaning of Section 501(a)(2)(B) of the Act, in that the methods and/or the controls used in manufacturing are not in conformance with cGMPs, as follows:

1. Manufacturing process validation for Liquichlor with Cerumene, Cerumite and Laxatone were found to be inadequate, in that:

   - The current retrospective review of validation data does not include justification of established process parameters, such as mixing and temperature ranges.
   - Particle size specifications have not been established for the active substances used in Liquichlor with Cerumene, Suspension.
   - There is no in-process testing to evaluate the effect of the colloid milling process on the active ingredients in suspension

RELEASE

REVIEWED BY Mercedes Mora 5/12/98
C.O. DATE

2. Laboratory controls and test procedures used for stability testing indicate variations in product potency, for which documented investigations were lacking, for example:

   - Liquichlor with Cerumene, Lot 9295 assay for chloramphenicol yielded 117% at the initial test station, 103% at 3 months and 124% at the 9 month test station.
   - Cerumite, Lot 3122, assay for Piperonyl Butoxide yielded 122% at the 12 month stability station.

3. The stability monitoring program, designed to assess the characteristics of drug products throughout expiry, is inadequate in that numerous test stations were missed or not performed, without justification, for example:

   - Liquicholor with Cerumene (18 month expiry) Lot 9252 missed assay at 9 months, Lot 9295 missed assay at 18 months.
   - Cerumite (36 month expiry) Lot 9412 missed assay at 6, 9 and 12 month intervals.
   - Laxatone (36 month expiry) Lot 9401 missed testing at 6, 9, and 12 month intervals.

4. There is no data to support the established holding times of bulk compounds for Liquichlor with Cerumene, in which procedures allow for a three week hold time prior to filling.

5. Cleaning validation studies have not yet been completed for all non-dedicated equipment which are currently used interchangeably in the compounding or filling of drug products, such as gels, non-aqueous and aqueous preparations.

6. The Quality Control Unit was found to be deficient in assuring that written procedures are being followed. for example:

   - Cerumite, Lot 9285, exceeded the established bulk holding time of two weeks and was released without being reassayed, per Time Limitations SOP 2-09.
   - Liquichlor Lot 9609, written procedures for establishing system suitability of the Gas Chromatographic (GC) instrument, requires the bracketing of sample with the standard before and after sample injection, was not followed for this lot.

The above list is not intended to be all-inclusive of deficiencies at your facility. It is your responsibility to ensure that the drug products you manufacture are in compliance with the Act and the regulations promulgated under it. You should take prompt action to correct these deficiencies. Failure to implement corrective measures may result in regulatory action, including seizure and/or injunction, without further notice.

We are in receipt of your written response, dated April 14, 1998. Our evaluation finds your response is generally unacceptable to address the cited FDA483 Observations. We offer the following comments in the order of the FDA483:

1. We disagree with your assertion that these products are retrospectively validated, based solely on products meeting finished product specifications. Your validation efforts should evaluate critical parameters, such as particle size specifications and in-process testing to determine the effects of the colloid milling process on active ingredients. We recognize that these products have been in production for over 20 years and therefore sufficient data should be available to conduct a retrospective evaluation for these products prior to your projected timeframe of August 1999.

2. This observation concerns the variable results obtained with the current GC method used in stability testing. These variable results indicate this method is unreliable in providing accurate and reproducible results in accordance with cGMP requirements. Your response references correspondence to CVM, submitted in 1979 and 1981, concerning the variation in analytical results for Liquichlor with Cerumene. This correspondence is not equivalent to documented laboratory investigations, which assesses the validity of the method employed and attempts to determine the assignable cause as it relates to errors in manufacturing or analytical technique.

3. While we acknowledge your commitment to employ all the resources necessary to ensure that stability studies are conducted as required, your response does not provide a corrective action plan on how this will be accomplished, for example, additional Quality Control monitoring and training.

4. If the data currently exists to support bulk holding times for each product, this should be available prior to your projected timeframe of September 30, 1998.

5. Incomplete or inadequate cleaning validation issues have been cited during inspections in conducted 1991 and 1995. We expect this issue will be resolved by your proposed timeframe of December 31, 1998.

6 – 8. Your corrective actions will be evaluated during the next inspection.

You should notify this office in writing, within 15 working days of receipt of this letter, of the additional steps you have taken to correct the noted deficiencies, including an explanation of each step being taken to prevent the recurrence of similar conditions. If corrective action cannot be completed within 15 working days, state the reason for the delay and timeframe within which corrections will be completed.

Your additional reply should be sent to the New Jersey District Office, FDA, 10 Waterview Blvd., 3rd Floor, Parsippany, New Jersey 07054, Atttention: Mercedes B. Mota, Compliance Officer.

Sincerely,

Douglas Ellsworth

Douglas Ellsworth, Director
New Jersey District. FDA